IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

KOTEWICZ *et al.*

Appl. No. *To be assigned*

Filed: *Herewith*

For: **Cloned Genes Encoding Reverse Transcriptase Lacking RNase H Activity**

Confirmation No. *To be assigned*

Art Unit: *To be assigned*

Examiner: *To be Assigned*

Atty. Docket: 0942.049000B/RWE/MTT

Letter to PTO Draftsman: Submission of Formal Drawings

Commissioner for Patents
Washington, D.C. 20231

Sir:

Submitted herewith are eight (8) sheets of formal drawings with Figures 1-4, 5A/5B, 6A, 6B, and 6C, corresponding to the informal drawings submitted with the above-captioned application. Acknowledgment of the receipt, approval, and entry of these formal drawings into this application is respectfully requested.

It is not believed that an extension of time is required, other than any already provided herewith. However, if an extension of time is needed to prevent abandonment of the application, then such extension of time is hereby petitioned. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036. A duplicate copy of this Letter is enclosed.

Respectfully submitted,
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Robert W. Esmond

Robert W. Esmond
Attorney for Applicants
Registration No. 32,893

Date: Dec. 21, 2001
1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600
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Appl. No *To be assigned* , Group Art Unit· *To be assigned*
Dkt No. 0942.490000B;
Inventors· KOTEWICZ *et al* ; Tel. 202/371-2600
Title. Cloned Genes Encodıng Reverse Transcrıptase Lacking
RNase Activıty

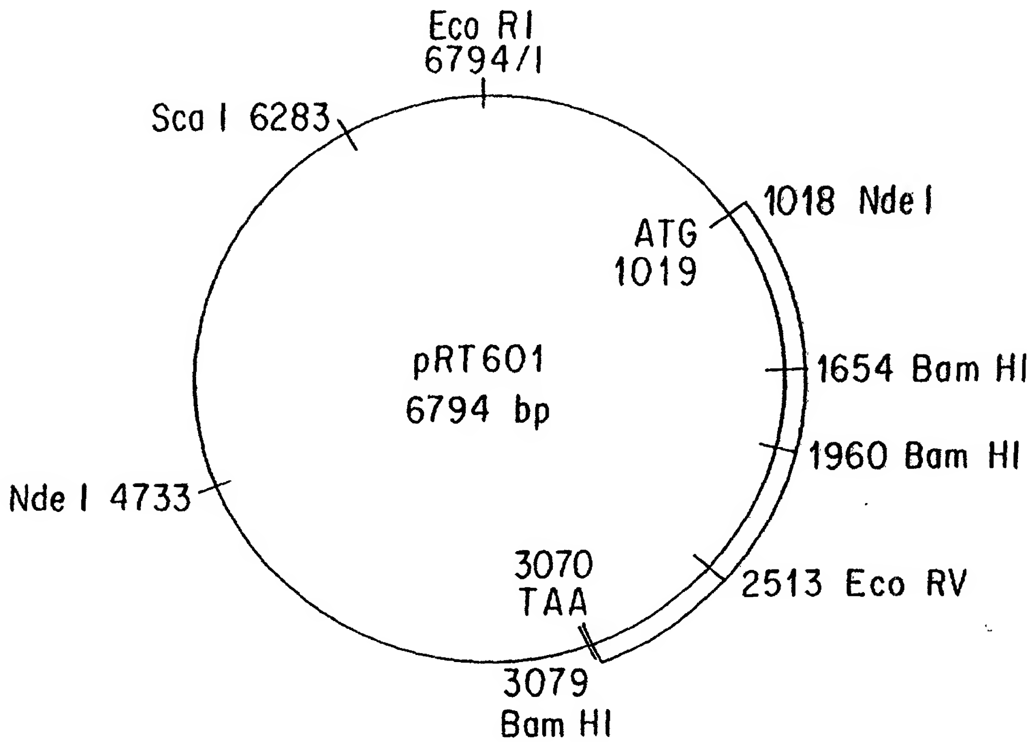

FIG. 1

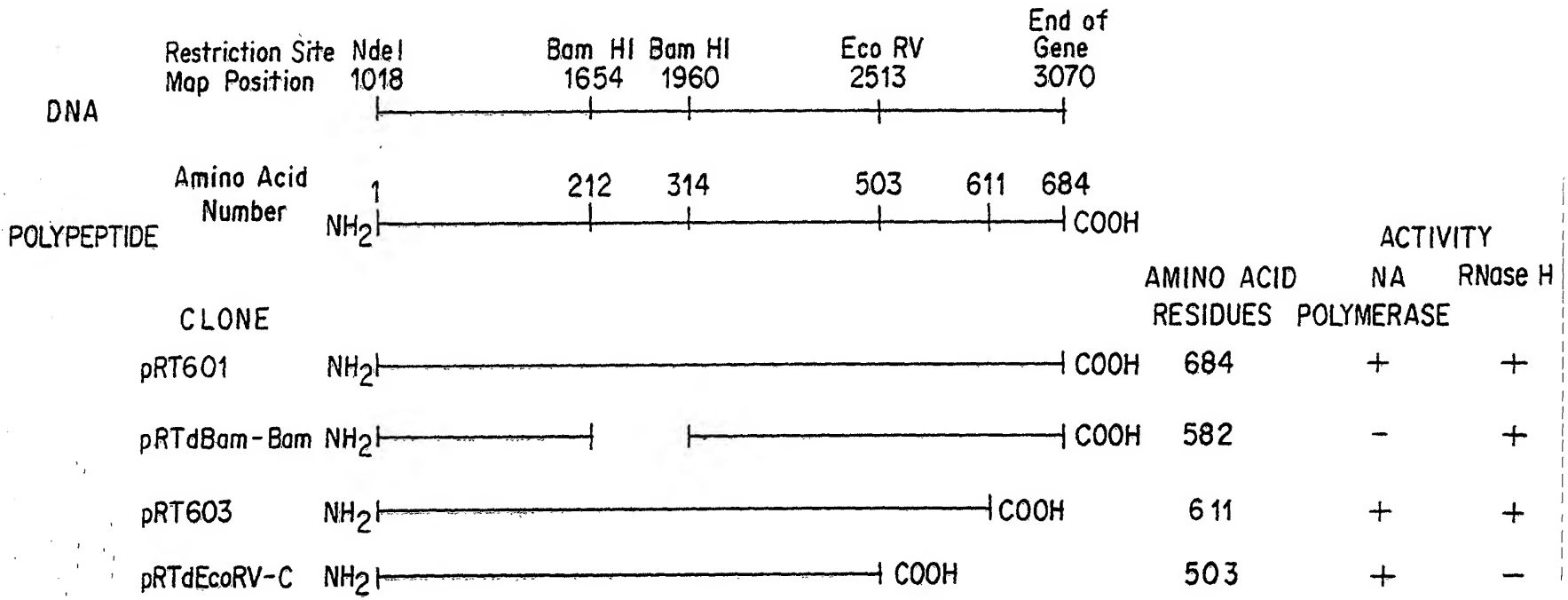

FIG. 2

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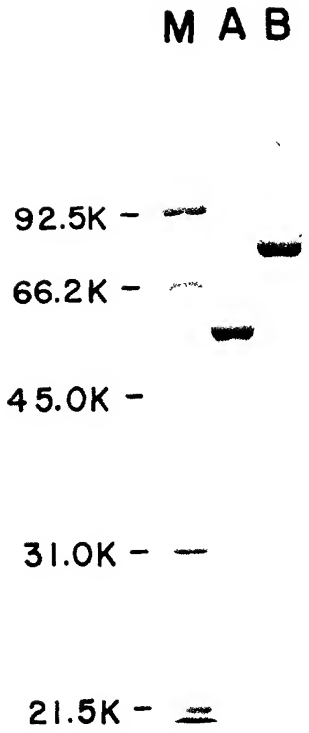

FIG. 3

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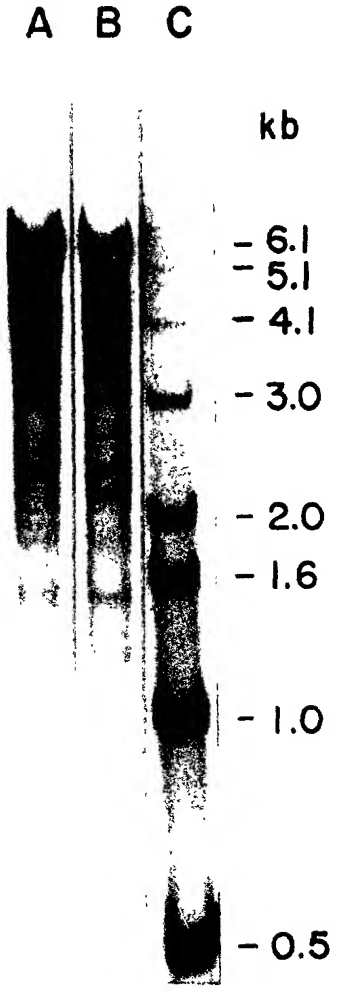

FIG. 4

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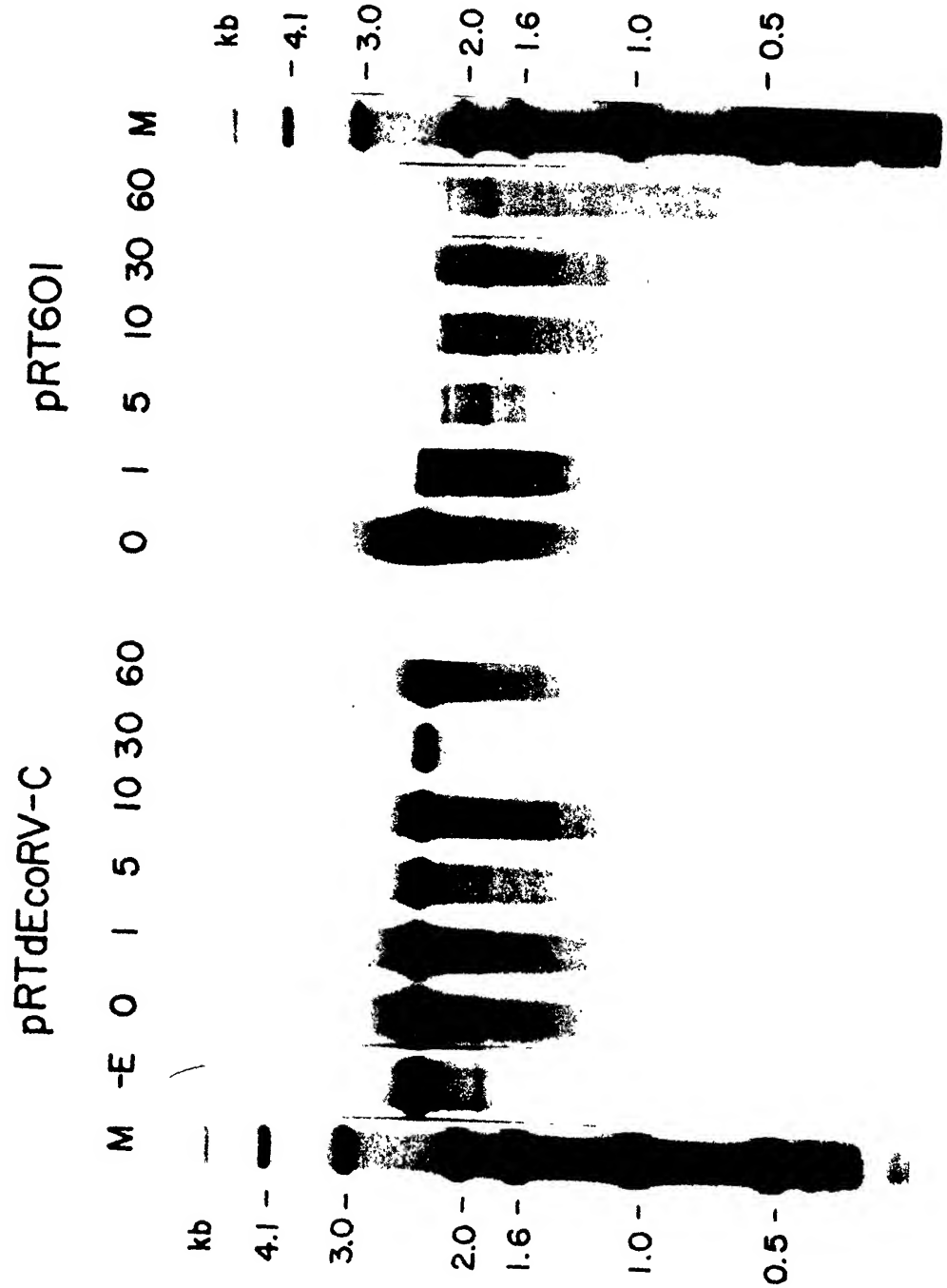

FIG. 5A

FIG. 5B

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1078
ATG ACC CTA AAT ATA GAA GAT GAG CAT CGG CTA CAT GAG ACC TCA AAA GAG CCA GAT GTT
MET Thr Leu Asn Ile Glu Asp Glu His Arg Leu His Glu Thr Ser Lys Glu Pro Asp Val

1138
TCT CTA GGG TCC ACA TGG CTG TCT GAT TTT CCT CAG GCC TGG GCG GAA ACC GGG GGC ATG
Ser Leu Gly Ser Thr Trp Leu Ser Asp Phe Pro Gln Ala Trp Ala Glu Thr Gly Gly MET

1198
GGA CTG GCA GTT CGC CAA GCT CCT CTG ATC ATA CCT CTG AAA GCA ACC TCT ACC CCC GTG
Gly Leu Ala Val Arg Gln Ala Pro Leu Ile Ile Pro Leu Lys Ala Thr Ser Thr Pro Val

1258
TCC ATA AAA CAA TAC CCC ATG TCA CAA GAA GCC AGA CTG GGG ATC AAG CCC CAC ATA CAG
Ser Ile Lys Gln Tyr Pro MET Ser Gln Glu Ala Arg Leu Gly Ile Lys Pro His Ile Gln

1318
AGA CTG TTG GAC CAG GGA ATA CTG GTA CCC TGC CAG TCC CCC TGG AAC ACG CCC CTG CTA
Arg Leu Leu Asp Gln Gly Ile Leu Val Pro Cys Gln Ser Pro Trp Asn Thr Pro Leu Leu

1378
CCC GTT AAG AAA CCA GGG ACT AAT GAT TAT AGG CCT GTC CAG GAT CTG AGA GAA GTC AAC
Pro Val Lys Lys Pro Gly Thr Asn Asp Tyr Arg Pro Val Gln Asp Leu Arg Glu Val Asn

1438
AAG CGG GTG GAA GAC ATC CAC CCC ACC GTG CCC AAC CCT TAC AAC CTC TTG AGC GGG CTC
Lys Arg Val Glu Asp Ile His Pro Thr Val Pro Asn Pro Tyr Asn Leu Leu Ser Gly Leu

1438
AAG CGG GTG GAA GAC ATC CAC CCC ACC GTG CCC AAC CCT TAC AAC CTC TTG AGC GGG CTC
Lys Arg Val Glu Asp Ile His Pro Thr Val Pro Asn Pro Tyr Asn Leu Leu Ser Gly Leu

1498
CCA CCG TCC CAC CAG TGG TAC ACT GTG CTT GAT TTA AAG GAT GCC TTT TTC TGC CTG AGA
Pro Pro Ser His Gln Trp Tyr Thr Val Leu Asp Leu Lys Asp Ala Phe Phe Cys Leu Arg

FIG.6A

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1558
CTC CAC CCC ACC AGT CAG CCT CTC TTC GCC TTT GAG TGG AGA GAT CCA GAG ATG GGA ATC
Leu His Pro Thr Ser Gln Pro Leu Phe Ala Phe Glu Trp Arg Asp Pro Glu MET Gly Ile

1618
TCA GGA CAA TTG ACC TGG ACC AGA CTC CCA CAG GGT TTC AAA AAC AGT CCC ACC CTG TTT
Ser Gly Gln Leu Thr Trp Thr Arg Leu Pro Gln Gly Phe Lys Asn Ser Pro Thr Leu Phe

1678
GAT GAG GCA CTG CAC AGA GAC CTA GCA GAC TTC CGG ATC CAG CAC CCA GAC TTG ATC CTG
Asp Glu Ala Leu His Arg Asp Leu Ala Asp Phe Arg Ile Gln His Pro Asp Leu Ile Leu

1738
CTA CAG TAC GTG GAT GAC TTA CTG CTG GCC GCC ACT TCT GAG CTA GAC TGC CAA CAA GGT
Leu Gln Tyr Val Asp Asp Leu Leu Leu Ala Ala Thr Ser Glu Leu Asp Cys Gln Gln Gly

1798
ACT CGG GCC CTG TTA CAA ACC CTA GGG AAC CTC GGG TAT CGG GCC TCG GCC AAG AAA GCC
Thr Arg Ala Leu Leu Gln Thr Leu Gly Asn Leu Gly Tyr Arg Ala Ser Ala Lys Lys Ala

1858
CAA ATT TGC CAG AAA CAG GTC AAG TAT CTG GGG TAT CTT CTA AAA GAG GGT CAG AGA TGG
Gln Ile Cys Gln Lys Gln Val Lys Tyr Leu Gly Tyr Leu Leu Lys Glu Gly Gln Arg Trp

1918
CTG ACT GAG GCC AGA AAA GAG ACT GTG ATG GGG CAG CCT ACT CCG AAG ACC CCT CGA CAA
Leu Thr Glu Ala Arg Lys Glu Thr Val MET Gly Gln Pro Thr Pro Lys Thr Pro Arg Gln

1978
CTA AGG GAG TTC CTA GGG ACG GCA GGC TTC TGT CGC CTC TGG ATC CCT GGG TTT GCA GAA
Leu Arg Glu Phe Leu Gly Thr Ala Gly Phe Cys Arg Leu Trp Ile Pro Gly Phe Ala Glu

2038
ATG GCA GCC CCC TTG TAC CCT CTC ACC AAA ACG GGG ACT CTG TTT AAT TGG GGC CCA GAC
MET Ala Ala Pro Leu Tyr Pro Leu Thr Lys Thr Gly Thr Leu Phe Asn Trp Gly Pro Asp

FIG.6B

Appl. No. *To be assigned* ; Group Art Unit: *To be assigned*
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2098
CAA CAA AAG GCC TAT CAA GAA ATC AAG CAA GCT CTT CTA ACT GCC CCA GCC CTG GGG TTG
Gln Gln Lys Ala Tyr Gln Glu Ile Lys Gln Ala Leu Leu Thr Ala Pro Ala Leu Gly Leu

2158
CCA GAT TTG ACT AAG CCC TTT GAA CTC TTT GTC GAC GAG AAG CAG GGC TAC GCC AAA GGT
Pro Asp Leu Thr Lys Pro Phe Glu Leu Phe Val Asp Glu Lys Gln Gly Tyr Ala Lys Gly

2218
GTC CTA ACG CAA AAA CTG GGA CCT TGG CGT CGG CCG GTG GCC TAC CTG TCC AAA AAG CTA
Val Leu Thr Gln Lys Leu Gly Pro Trp Arg Arg Pro Val Ala Tyr Leu Ser Lys Lys Leu

2278
GAC CCA GTA GCA GCT GGG TGG CCC CCT TGC CTA CGG ATG GTA GCA GCC ATT GCC GTA CTG
Asp Pro Val Ala Ala Gly Trp Pro Pro Cys Leu Arg MET Val Ala Ala Ile Ala Val Leu

2338
ACA AAG GAT GCA GGC AAG CTA ACC ATG GGA CAG CCA CTA GTC ATT CTG GCC CCC CAT GCA
Thr Lys Asp Ala Gly Lys Leu Thr MET Gly Gln Pro Leu Val Ile Leu Ala Pro His Ala

2398
GTA GAG GCA CTA GTC AAA CAA CCC CCC GAC CGC TGG CTT TCC AAC GCC CGG ATG ACT CAC
Val Glu Ala Leu Val Lys Gln Pro Pro Asp Arg Trp Leu Ser Asn Ala Arg MET Thr His

2458
TAT CAG GCC TTG CTT TTG GAC ACG GAC CGG GTC CAG TTC GGA CCG GTG GTA GCC CTG AAC
Tyr Gln Ala Leu Leu Leu Asp Thr Asp Arg Val Gln Phe Gly Pro Val Val Ala Leu Asn

2518
CCG GCT ACG CTG CTC CCA CTG CCT GAG GAA GGG CTG CAA CAC AAC TGC CTT GAT AAT TCC
Pro Ala Thr Leu Leu Pro Leu Pro Glu Glu Gly Leu Gln His Asn Cys Leu Asp Asn Ser

2533
CGC TTA ATT AAT TAA
Arg Leu Ile Asn

FIG. 6C

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Preliminary Amendment

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution of the captioned application, Applicants submit the following Preliminary Amendments and Remarks. This Preliminary Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.111 and MPEP 714; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R.

§ 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036

Amendments

Please amend the application as follows:

In the Specification:

In the specification at page 10, please delete the fifth and sixth full paragraphs, and substitute therefor the following paragraphs:

Figs. 5A and 5B. These figures depict an autoradiogram of ^{32}P-labeled 2.3 kb poly(A)-tailed RNA after oligo(dT)-primed cDNA synthesis catalyzed by pRTdEcoRV-C RT or pRT601 RT. Aliquots were removed from reaction mixtures containing no enzyme (-E) or 200 units of RT at the times indicated (in min). The minus enzyme control was incubated for 60 min. Samples were electrophoresed as described in Materials and Methods. A 1 kb ladder was used as marker (M).

Figs. 6A, 6B, and 6C. These figures depict the DNA sequence which encodes reverse transcriptase having DNA polymerase activity and substantially no RNase H activity. Also shown is the corresponding amino acid sequence.

In the specification at page 15, please delete the first full paragraph, and substitute therefor the following paragraph:

According to these methods, the portion of the RT gene derived from M-MLV which encodes DNA polymerase was localized to about 1495 base pairs (about 1018 to about 2512)

as shown in Figs. 6A, 6B, and 6C. The protein expressed by this gene has about 503 amino acids (Figs. 6A, 6B, and 6C). This protein has DNA polymerase activity and substantially no RNase H activity.

In the specification at pages 26-27, please delete the bridging paragraph, and substitute therefor the following paragraph:

To confirm that pRTdEcoRV-C RT completely lacked RNase H activity, the integrity of a uniformly ^{32}P-labeled RNA template after conversion to hybrid form during RT-catalyzed DNA synthesis was examined. Figs. 5A and 5B show that with pRT601 RT, the full-length 2.3 kb RNA template was degraded totally after 5 min of synthesis. In contrast, with pRTdEcoRV-C RT the RNA was intact even after 60 min. The amount of cDNA synthesized after 60 min from 1 μg of RNA was 0.67 and 0.76 μg with pRT601 and pRTdEcoRV-C RT, respectively. When 10 units of E. coli RNase H were added to the pRTdEcoRV-C RT reaction after 60 min of incubation, all of the RNA was degraded, confirming the hybrid state of the RNA. In addition, 15 μg (1,200 units) of pRTdEcoRV-C RT solubilized no radioactivity from a $[^3H](A)_n \cdot (dT)_n$ substrate in which the $[^3H](A)_n$ had a specific activity of 2,200 cpm/pmole (Materials and Methods).

In the Claims:

Please amend the claims as follow:

Please cancel claims 2-23 without prejudice to the right to prosecute the subject matter of these claims in one or more continuing or divisional applications.

Remarks

By the foregoing amendments, claims 2-23 have been cancelled without prejudice or disclaimer. Upon entry of the foregoing amendments, claim 1 is pending in the application and is the independent claim. Applicants respectfully assert that no new matter has been entered by these amendments.

It is believed that the present application is in condition for immediate examination. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Robert W. Esmond

Robert W. Esmond
Attorney for Applicants
Registration No. 32,893

Date: Dec. 21, 2001

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

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SKGF Rev. 3/16/01

Version with markings to show changes made

In the Specification:

In the specification at page 10, please delete the fifth and sixth full paragraphs, and substitute therefor the following paragraphs:

[Figure 5. This figure depicts] Figs. 5A and 5B. These figures depict an autoradiogram of ^{32}P-labeled 2.3 kb poly(A)-tailed RNA after oligo(dT)-primed cDNA synthesis catalyzed by pRTdEcoRV-C RT or pRT601 RT. Aliquots were removed from reaction mixtures containing no enzyme (-E) or 200 units of RT at the times indicated (in min). The minus enzyme control was incubated for 60 min. Samples were electrophoresed as described in Materials and Methods. A 1 kb ladder was used as marker (M).

[Figure 6. This figure depicts] Figs. 6A, 6B, and 6C. These figures depict the DNA sequence which encodes reverse transcriptase having DNA polymerase activity and substantially no RNase H activity. Also shown is the corresponding amino acid sequence.

In the specification at page 15, please delete the first full paragraph, and substitute therefor the following paragraph:

According to these methods, the portion of the RT gene derived from M-MLV which encodes DNA polymerase was localized to about 1495 base pairs (about 1018 to about 2512) as shown in [Figure 6] Figs. 6A, 6B, and 6C. The protein expressed by this gene has about 503 amino acids ([Figure 6] Figs. 6A, 6B, and 6C). This protein has DNA polymerase activity and substantially no RNase H activity.

In the specification at pages 26-27, please delete the bridging paragraph, and substitute therefor the following paragraph:

To confirm that pRTdEcoRV-C RT completely lacked RNase H activity, the integrity of a uniformly ^{32}P-labeled RNA template after conversion to hybrid form during RT-catalyzed DNA synthesis was examined. [Figure 5 shows] Figs. 5A and 5B show that with pRT601 RT, the full-length 2.3 kb RNA template was degraded totally after 5 min of synthesis. In contrast, with pRTdEcoRV-C RT the RNA was intact even after 60 min. The amount of cDNA synthesized after 60 min from 1 μg of RNA was 0.67 and 0.76 μg with pRT601 and pRTdEcoRV-C RT, respectively. When 10 units of E. coli RNase H were added to the pRTdEcoRV-C RT reaction after 60 min of incubation, all of the RNA was degraded, confirming the hybrid state of the RNA. In addition, 15 μg (1,200 units) of pRTdEcoRV-C RT solubilized no radioactivity from a $[^3H](A)_n \cdot (dT)_n$ substrate in which the $[^3H](A)_n$ had a specific activity of 2,200 cpm/pmole (Materials and Methods).

In the Claims:

Claims 2-23 have been cancelled.